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FURTHER STUDIES ON THE RELATION BETWEEN MITOCHONDRIA AND GLYCOLYSIS

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ABSTRACT. The relation between mitochondria and glycolysis is studied. It is found that mitochondria influences glycolysis even when glucose alone is used as the substrate, and not combined with HDP.

We previously reported on the limitation of anaerobic glycolysis of /446
highly active tissue extracts by addition of large amounts of mitochondria, and strong stimulation of the formation of lactic and pyruvic acids by lower mitochondrial concentrations [1,2]. Since then, Aisenberg et al. [3] reported on limitation of glycolysis by mitochondria under aerobic conditions. They considered that a function of this organelle related to respiration, in the sense of the Pasteur effect, was responsible. Szekely [4] also described the stimulating action of liver mitochondria on glycolysis of erythrocyte extracts, which was supposed to be simultaneously related to the respiratory activity of the mitochondria. Consequently, we shall give our views on these two results which differ from our own results, in which there was not only limitation but also stimulation of glycolysis anaerobically.

The glycolytic system used was a highly active supernatant (1.0 ml per Warburg vessel) of a rat brain extract in isotonic KCl (1:5). To this, we added mitochondria isolated at 0° in 0.25 molar sucrose from rat liver, hepatoma, Jensen sarcoma, and Ehrlich carcinoma, in quantities of 2.3 to 300 milligrams fresh weight, suspended in an isotonic KCl solution (pH 7.4). The side arms contained ATP, DPN, nicotinamide, $KHCO_3$, and $MgCl_2$ as well as substrate, which was usually glucose alone or glucose plus hexosediphosphate (HDP). The tests were performed in parallel flasks both aerobically (air) and anaerobically (oxygen-free nitrogen). Incubation was for one-half hour at 38°. Lactic acid, pyruvic acid, and glucose were determined chemically.

*Numbers in the margin indicate pagination in the original foreign text.

Results: With large amounts of mitochondria (75 to 300 mg per vessel) from liver, hepatoma, Jensen sarcoma, and Ehrlich carcinoma, the formation of lactic and pyruvic acid was strongly, and usually even completely, inhibited in comparison to the corresponding vessels without addition of mitochondria, under aerobic as well as anaerobic conditions. This inhibition is particularly distinct if glucose is used exclusively as the substrate. Simultaneously with the inhibition of glycolysis, there is strong restriction of glucose consumption, even with the simultaneous presence of HDP. Lower concentrations of mitochondria (18.8 to 37.5 mg) cause the strong stimulation of lactic and pyruvic acid formation, likewise both anaerobically and aerobically, with simultaneous strong stimulation of sugar disappearance. This is considerably greater than that which corresponds to the equivalent amounts of lactic and pyruvic acid formed. It also occurs if glucose and HDP are used simultaneously as substrates.

It was possible to exclude extreme DPN splitting by the DPNase of the mitochondria and the glycolytic system as a cause, particularly for glycolysis limitation at high mitochondrial concentrations. This was done by DPN determinations (optical test after enzymatic hydrolysis) after the incubation.

Thus it appears that the effect which we have observed for mitochondria on glycolysis, in the sense of inhibition by large amounts and stimulation by small amounts, occurs not only anaerobically but also aerobically. The somewhat greater inhibition under aerobic conditions can be explained by the oxidation of the end products of glycolysis by the mitochondria. Furthermore, these experiments supported the finding which we emphasized previously [1b] that the influence of mitochondria on glycolysis occurs even when glucose alone is used as the substrate, and not solely in combination with HDP. In comparison vessels with the same amounts of mitochondria, we have not yet been able to demonstrate specific differences in the action of normal and tumor mitochondria. But it should be noted that the tumor cells usually contain significantly less mitochondria than the homologous normal cells (e.g.,

hepatoma and liver), so that the conditions for stimulation of glycolysis may perhaps occur in the tumor cell, while in the normal cell rich in mitochondria there may be inhibition of glycolysis by the mitochondria. After a biochemical consideration of our results, we continue to maintain the decisive significance of ATPase [1,2].

REFERENCES

1a. Graffi, A. and E. J. Schneider. Naturwiss. Vol. 43, 1956, p. 376.

1b. —. Z. arztl. Fortbildg., Vol. 50, 1956, p. 760.

2a. Graffi, A, E. J. Schneider and G. Sydow. Naturwiss. Vol. 43, 1956, p. 472.

2b. —. Z. arztl. Fortbildg. Vol. 50, 1956, p. 1026.

3. Aisenberg, A. C., B. Reinfarje and V. R. Potter. J. of Biol. Chem. Vol. 224, 1957, p. 1099.

4. Szekely, M. and T. Varady. Acta Physiol. Acad. Sci. Hung. Vol. 8, 1955, p. 303.

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